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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Gates & Cooper LLP
Howard Hughes Center
6701 Center Drive West, Suite 1050
Los Angeles, CA 90045

EXAMINER
FALK, ANNE MARIE

ART UNIT	PAPER NUMBER
1632	13

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/581,308	NALDINI ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 February 2001* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed June 12, 2003 (Paper No. 12) has been entered. Claims 1-3 have been amended. Claims 5-12 have been newly added.

Accordingly, Claims 1-12 are pending in the instant application.

The following rejections are reiterated or newly applied and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous office action are hereby withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 stand rejected and Claims 5, 7, 9, 10, and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by U.S. Patent No. 5,650,309 (Wong-Staal et al., issued July 22, 1997).

The claims are directed to a method for treating a host infected with a lentivirus by exposing the host to a lentivirus vector, wherein the lentivirus vector has an intact 5' lentivirus LTR. No specific treatment effect is recited in the claims.

Wong-Staal et al. disclose an HIV-based vector useful for inhibiting viral replication in a cell. See Example 1, Columns 16-17. The HIV-LTR was shown to drive expression of the reporter construct (Column 16, lines 7-8). The vector disclosed qualifies as a lentiviral vector, as recited in the claims.

At page 6, paragraph 6 of the response, Applicants argue that Wong-Staal does not teach a method of treating lentivirus infection in a host by exposing the host to a lentivirus vector having an intact 5' LTR. On the contrary, Wong-Staal specifically teaches that the disclosed vectors stably transduce cells and render the cells resistant to a target virus (Column 2, lines 1-13). Wong-Staal states that the vectors block or ameliorate "infection by the target virus within the host (Column 2, lines 11-13). Furthermore, it is noted that the instant claims do not require any treatment effect. Rather the claims only require exposing a host to a lentivirus vector. Furthermore, Wong-Staal explicitly teaches that "[t]he vector can be administered directly to the organism for transduction of cells *in vivo* ... to treat virally-mediated diseases such as AIDS in patients." (Column 10, lines 43-48).

At page 7, paragraph 1 of the response, Applicants argue that Wong-Staal teaches that when the virus is derived from HIV, the LTR is modified. This is not entirely correct because the specification teaches that the LTR may or may not be modified. The relevant section to which Applicants refer states that

> "[w]here the replication defective portion of the virus is derived from an HIV virus, the replication defective, rescuable HIV genome would be rendered replication defective by modifying the HIV promoter region (e.g., the HIV LTR), **or by deleting or modifying a gene or genes whose product is necessary for viral replication**, such as a gene encoding a protein necessary for transcription of the virus or a viral structural protein, including the tat, rev, gag, pol, env, vif, vpr, nef, and vpu/vpx genes." (Column 2, lines 48-56, emphasis added).

Furthermore, the specification teaches that in, a preferred embodiment, the anti-HIV gene is under the control of the HIV 5' LTR (Column 15, lines 54-57). Figures 4, 6, 8, 10, and 12 depict constructs having an intact 5' LTR.

At page 7, paragraph 1 of the response, Applicants argue that Wong-Staal teaches away from the claimed invention because the therapeutic vector explicitly requires both a cellular transducing portion and an antiviral portion. However, the claims being rejected here clearly read on the method used by Wong-Staal because there is nothing in the claims to exclude the use of a vector comprising an antiviral gene. Furthermore, instant Claim 11 explicitly requires that the lentivirus vector contain a transgene.

Claim 1-3 stand rejected and Claims 5, 7, 9, 10, and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,650,309 (Wong-Staal et al., filed May 16, 1995), for reasons of record advanced on page 4 of the Office Action of Paper No. 10 (mailed 2/11/03) and as further discussed herein above.

Claims 1-4 stand rejected and Claims 5-7 and 9-12 are rejected under 35 U.S.C. 102(a) as being anticipated by U.S. Patent No. 5,665,577 (Sodroski et al., issued September 9, 1997).

The claims are directed to a method for treating a host infected with a lentivirus by exposing the host to a lentivirus vector, wherein the lentivirus vector has an intact 5' LTR. No specific treatment effect is recited in the claims.

Sodroski et al. disclose an HIV-based vector useful for developing a vaccine for HIV. The HIV vector preferentially uses the HIV-1 LTR as the promoter. See Claim 10. The vector disclosed qualifies as a lentiviral vector, as recited in the claims.

At page 7, paragraph 2 of the response, Applicants argue that Sodroski fails to teach treating lentivirus infection in a host by exposing the host to a lentivirus vector having an intact 5' LTR. This argument is not persuasive because Sodroski specifically teaches that the virions produced from the disclosed vectors can be used for vaccines and as a system for efficiently introducing a desired gene into a mammalian cell (Column 3, lines 23-26). Thus, the reference clearly discloses that the vectors are to be

used for *in vivo* administration. Furthermore, the instant claims do not require any treatment effect, but rather only require exposing a host to a lentivirus vector.

At page 7, paragraph 2 of the response, Applicants argue that Sodroski teaches away from the claimed invention because it describes the need for combinations of vectors. However, there is nothing in the claims to exclude the use of combinations of vectors. Furthermore, the discussion at Column 3, lines 16-26 makes it clear that a vaccine would consist only of a virion produced by packaging negative proviruses, not a combination of vectors.

Claims 1-4 stand rejected and Claims 5-7 and 9-12 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,665,577 (Sodroski et al., filed February 6, 1989) for reasons of record advanced on page 5 of the Office Action of Paper No. 10 (mailed 2/11/03) and as further discussed herein above.

Claims 1, 3-7 and 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Poeschla (1996).

Poeschla et al. disclose HIV-based vectors useful for inhibiting viral replication in a cell. The reference discloses HIV-1 and HIV-2 based vectors comprising an intact 5' LTR (see Figure 2 and the paragraph bridging pages 11397-11398). The reference further discloses that the vectors comprise their respective *rev* response element (RRE) (p. 11398, paragraph 1). The reference discloses that the vectors are for use in HIV gene therapy (see Figure 1). Thus, the reference clearly directs one of skill in the art to administer the vectors to an HIV-infected subject for the purpose of producing a treatment effect.

Thus, the claimed invention is disclosed in the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 stand rejected and Claims 5-7 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Irwin et al. (1994).

The claims are directed to a method for treating a host infected with a lentivirus by exposing the host to a lentivirus vector, wherein the lentivirus vector has an intact 5' LTR. No specific treatment effect is recited in the claims.

Irwin et al. (1994) disclose that direct injection of a lentiviral vector encoding HIV-1 proteins into mice and nonhuman primates produced an HIV-specific CTL immune response. Although the animals were not infected with HIV-1, the authors pointed out that the results of the studies demonstrate that the retrovector immunization method can be used to induce or augment CTL responses in HIV-1-infected individuals.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

At page 7, paragraph 3, Applicants argue that Irwin describes injection of recombinant retroviral vectors carrying HIV-1 rev and env genes into muscle and a subsequent CTL response. Applicants assert that this reference does not suggest treating a lentivirus infection in a host by exposing the host to a lentivirus vector having an intact 5' LTR. No support is offered for this assertion. Furthermore, the reference explicitly states that the results of the studies demonstrate that the retrovector immunization method can be used to induce or augment CTL responses in HIV-1-infected individuals (see abstract).

Claims 1-4 stand rejected and Claims 5-7 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naldini et al. (1996) and Irwin et al. (1994).

The claims are directed to a method for treating a host infected with a lentivirus by exposing the host to a lentivirus vector, wherein the lentivirus vector has an intact 5' LTR. No specific treatment effect is recited in the claims.

Naldini et al. (1996) disclose that an HIV-derived retroviral vector was used to transduce nondividing cells. The vector contained an intact 5' LTR (see Figure 1). Naldini et al. does not describe the use of this vector in the treatment of a lentiviral-infected host.

Irwin et al. (1994) disclose that direct injection of a lentiviral vector encoding HIV-1 proteins into mice and nonhuman primates produced an HIV-specific CTL immune response. Although the animals were not infected with HIV-1, the authors pointed out that the results of the studies demonstrate that the retrovector immunization method can be used to induce or augment CTL responses in HIV-1-infected individuals.

Since one of skill in the art would have been motivated to provide a method for treating an HIV infection, the skilled artisan would have been motivated to combine the teachings of Naldini et al. and Irwin et al., wherein the HIV-derived vector of Naldini et al. was modified to encode HIV-1 proteins as demonstrated by Irwin et al. to thereby efficiently infect human cells and produce an HIV-specific CTL immune response in HIV-1-infected individuals.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

At page 7, paragraph 3 of the response, Applicants argue that Naldini describes a lentiviral transfer vector capable of delivering a gene to a cell. Applicants assert that the Naldini and Irwin references in combination do not suggest treating a lentivirus infection in a host by exposing the host to a lentivirus vector having an intact 5' LTR. No support is offered for this assertion. It is maintained that

one of skill in the art would have been motivated to provide a method for treating an HIV infection by modifying the HIV-derived vector of Naldini et al. to encode HIV-1 proteins as demonstrated by Irwin et al. to thereby efficiently infect human cells and produce an HIV-specific CTL immune response in HIV-1 infected individuals.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,650,309 (Wong-Staal et al.).

Claim 8 is directed to a method for treating a host infected with a lentivirus by exposing the host to a lentivirus vector, wherein the lentivirus vector has an intact 5' LTR, wherein the lentivirus vector has 124 base pairs of nef sequences upstream of the 3' LTR replaced with a polylinker. No specific treatment effect is recited in the claims.

Wong-Staal states that

> "[w]here the replication defective portion of the virus is derived from an HIV virus, the replication defective, rescuable HIV genome would be rendered replication defective by modifying the HIV promoter region (e.g., the HIV LTR), **or by deleting or modifying a gene or genes whose product is necessary for viral replication**, such as a gene encoding a protein necessary for transcription of the virus or a viral structural protein, including the tat, rev, gag, pol, env, vif, vpr, nef, and vpu/vpx genes." (Column 2, lines 48-56, emphasis added).

Although the reference does not explicitly direct replacing 124 base pairs of nef sequence with a polylinker, given the suggestion by Wong-Staal to delete the nef gene, one of skill in the art would recognize that any genetic manipulation that results in inactivation of the nef gene would successfully achieve the goal of producing a replication defective genome.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, William Phillips, whose telephone number is (703) 305-3482.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER